Remarks

Favorable consideration of this application is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-12 and 14-20 are pending in the application. Claims 1-12 and 14-20 have been rejected. Claim 1 has been amended, support for which can be found as described below. No new matter has been added.

Rejection Under 35 USC §112, First Paragraph- Written Description

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner states the following:

> It is maintained that detailed structural knowledge of any alternatively spliced gene products is a requisite for producing an siRNA double stranded nucleic acid having at least 95% sequence identity to a common nucleic acid shared by two or more isoforms of said gene products and further producing a specific isoform having one or more mismatches relative to said double stranded portion of said nucleic acid.

Without acquiescing to the Examiner's arguments, Applicants have amended independent claim 1 to include the additional first step of "determining, from a gene product of interest, a specific isoform of interest from said gene product, and isoforms of said gene product not of interest." By so doing, Applicants have ensured that practitioners of the claimed methods of the invention possess knowledge of the isoforms of the gene products of interest. Even though Applicants, as explained below, remain of the opinion that ordinarily skilled practitioners already possess said knowledge, and would not be interested in employing the claimed methods without said knowledge, the claim amendment is an additional way to provide support for the present claims.

Support for the claim amendment can be found, among other places, in paragraph [0044] of the present specification, in the terms "desired" and "undesired." These terms presuppose a level of knowledge about the gene product of interest, that some isoforms are more desirable than others for purpose of in vitro experimentation. One cannot discern "desired" isoforms from "undesired" without having conducted research and/or experimentation into the sequence of her gene product of interest. The terms "desired" and "undesired" no longer appear in claim 1, and have instead been replaced by "specific isoform" and "other isoforms" as per the Examiner's earlier requests, in order to facilitate prosecution. The terms remain an integral part of the invention, however, and provide support for the amendment to claim 1.

Additional support for the claim amendment can be found in paragraph [0046] of the present invention. Said paragraph discusses commonly used techniques of sequence analysis, identification, and comparison that can easily be used for the newly-added "determination" step of amended claim 1. Sequence analysis techniques described in paragraph [0046] can be used to determine "desired" and "undesired" isoforms from gene products of interest, and to distinguish them from one another.

Applicants reiterate their past arguments, including that the gene products themselves (e.g., the encoded proteins) are not essential to the claimed methods of the invention, and that there is no substantial variation within the claimed genus- i.e., practitioners of the claimed invention are interested in the nucleic acids of the present claims only in terms of the presence and number of their isoforms, and the nucleic acid sequences thereof, and not in terms of the gene products encoded thereby. Applicants also reiterate the applicability of the following from Example 18 of the Written Description Guidelines: "The art indicates that there is no substantial variation within the genus because there are a limited number of ways to practice the process steps of the claimed invention," and posit that the steps of the claimed methods are similarly applied to all nucleic acids with one or more isoforms, irrespective of the gene products encoded thereby.

Applicants also reiterate prior arguments that a practitioner of the methods of the invention only needs to possess knowledge relating to her gene product of interest (as opposed to knowledge about every possible gene product within the claimed methods), and that one would already possess said information before employing the presently claimed methods.

Rejection Under 35 USC §112, First Paragraph- Enablement

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide an enablement for the full scope of the invention. Applicants respectfully thank the Examiner for acknowledging that the last claim amendment(s) (addition of "in vitro") addressed the enablement rejection in part. Applicants respectfully disagree, however, with the Examiner's contention that there remain "additional issues regarding the unpredictability of attenuating expression of numerous target genes by RNAi in different cell types for which adequate structural details need to be determined," and which would require undue experimentation.

Applicants have added a first step to claim 1, of "determining, from a gene product of interest, a specific isoform of interest from said gene product, and isoforms of said gene product not of interest." As described above, this step requires an analysis (e.g., a sequence

analysis) on the part of the practitioner of the method claims of the invention. This analysis includes a determination of isoforms of interest (i.e., "desired" isoforms) versus isoforms not of interest (i.e., "undesired" isoforms). As part of this determination, practitioners ascertain which inhibitory ribonucleic acid sequences (which overlap between desired and undesired isoforms) are most likely to successfully knock down the undesired isoforms and leave the mismatched, desired isoforms remaining. The best inhibitory ribonucleic acid sequences are determined without undue experimentation and used according to the present invention.

Rejection Under 35 USC §102(e)

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §102(e), as anticipated by Tuschl et al. (U.S. Patent Publn. No.: 2004/0259247)(hereafter, "the Tuschl reference"). Although the Tuschl reference and the claims of the present invention are similar in that both pertain to RNAi, Applicants respectfully disagree that the Tuschl reference anticipates the present claims. In fact, Applicants cite Tuschl publications related to the Tuschl patent application reference in the present application, as a way of describing past contributions to the RNAi field before distinguishing the present methods of the invention from any of the Tuschl work described. Applicants recognize that not every element of claims 1-12 and 14-20 is met by the Tuschl reference, and therefore respectfully request withdrawal of the §102(e) rejection.

The Tuschl reference describes using RNAi to inhibit the expression of endogenous target genes, thereby knocking them out (i.e., suppressing their function); on the other hand, the present invention contemplates inhibiting isoforms of a gene of interest, while protecting isoforms of interest of the gene of interest. Critically, the latter allows for the investigation of the function of individual gene isoforms, while the former does not.

Tuschl pertains to therapeutic treatment, as opposed to the kind of investigation and analysis engendered by the present method claims. For instance, beginning with paragraphs [0030] of US2004/0259247, the Tuschl reference describes target genes as associated with pathology, the administration of RNAi via pharmaceutical compositions, and therapeutic applications. The present claims, in their amended state, describe in vitro analytical techniques best suited for the study of certain desired isoforms of gene products of interest (and said techniques are facilitated by the isolation of said desired isoforms).

Applicants respectfully request entry of the amendments to the claims and the specification and submit no new matter is added thereby. Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,

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